

SEQUENCE LISTING

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<110> SOLARI, ROBERTO CELESTE ERCOLE
     CHAMPION, BRIAN ROBERT
     WARD, GEORGE ALBERT
<120> CONJUGATE OF A TRANSPORT PROTEIN AND A PROTEIN FOR
     MODULATION OF NOTCH SIGNALLING
<130> 674525-2007
<140> 10/720,896
<141> 2003-11-24
<150> PCT/GB02/02438
<151> 2002-05-24
<150> GB 0112818.0
<151> 2001-05-25
<160> 17
<170> PatentIn Ver. 3.3
<210> 1
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<212> DNA
<213> Artificial Sequence
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      for amplifying HES1 promoter from mouse genomic DNA
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<212> DNA
<213> Artificial Sequence
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<220> <223>	Description of Artificial Sequence: Synthetic Adenovirus major late promoter TATA-box motif with BglII and HindIII cohesive ends	
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<211> 31
<212> DNA
<213> Artificial Sequence
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      amplimer for generating a truncated fragment of
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<211> 91
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Synthetic Oligo
      annealed to the NIC2202 sequence to remove the stop codon
      from theNIC2202 fragment of human Notchl cDNA
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<210> 10
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<213> Artificial Sequence
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<212> PRT
<213> Homo sapiens
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<222> (891)

<223> Variable amino acid

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Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys 35 40 45

Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu 50 60

Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg 65 70 75 80

Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro 85 90 95

Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg 100 105 110

Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg 115 120 125

Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys 130 135 140

Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala 145 150 155 160

Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg 165 170 175

Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly 180 185 190

Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala 195 200 205

Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro 210 215 220

Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr 225 230 240

His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu 245 250 255

Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys 260 265 270

- Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr 275 280 285
- Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn 290 295 300
- Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn 305 310 315 320
- Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile 325 330 335
- Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp 340 345 350
- Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu 355 360 365
- Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly 370 375 380
- Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys 385 390 395 400
- Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys 405 410 415
- Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr 420 425 430
- Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg 435 440 445
- Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp 450 455 460
- Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met 480
- Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser 485 490 495
- Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe 500 505 510
- Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp 515 520 525
- Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu 530 535 540
- Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly 545 550 555 560
- Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His
 565 570 575

Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg 580 585 590

Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser 595 600 605

Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala 610 615 620

Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile 625 630 635 640

Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu 645 650 655

Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly 660 665 670

Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His 675 680 685

Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys 690 695 700

Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys 705 710 715 720

Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly 725 730 735

Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
740 745 750

Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
755 760 765

Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser

Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys 785 790 795 800

Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn 805 810 815

Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro 820 825 830

Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu 835 840 845

Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly 850 860

Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg 865 870 875 880

- His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys 885 890 895
- Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys 900 905 910
- Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn 915 920 925
- Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu 930 940
- Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn 945 950 955 960
- Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe 965 970 975
- Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser 980 985 990
- Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys 995 1000 1005
- Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val Asn
- Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln Asp Gly 1025 1030 1035 1040
- Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr Gly Pro Asn 1045 1050 1055
- Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro Cys Lys Asn Gly
 1060 1065 1070
- Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg Cys Glu Cys Pro Ser
- Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro Ser Val Ser Cys Glu Val 1090 1095 1100
- Ala Ala Gln Arg Gln Gly Val Asp Val Ala Arg Leu Cys Gln His Gly 1105 1110 1115 1120
- Gly Leu Cys Val Asp Ala Gly Asn Thr His His Cys Arg Cys Gln Ala 1125 1130 1135
- Gly Tyr Thr Gly Ser Tyr Cys Glu Asp Leu Val Asp Glu Cys Ser Pro 1140 1145 1150
- Ser Pro Cys Gln Asn Gly Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr 1155 1160 1165
- Ser Cys Lys Cys Val Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu 1170 1175 1180

- Ile Asp Glu Cys Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu 1185 1190 1195 1200
- Asp Leu Pro Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly 1205 1210 1215
- Val His Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro 1220 1225 1230
- Val Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln 1235 1240 1245
- Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu Arg 1250 1255 1260
- Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp Ala Arg 1265 1270 1275 1280
- Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His Cys Glu Cys 1285 1290 1295
- Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val Ile Asn Gly Cys 1300 1305 1310
- Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys Ala Val Ala Ser Asn 1315 1320 1325
- Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro Ala Gly Phe Glu Gly Ala 1330 1335 1340
- Thr Cys Glu Asn Asp Ala Arg Thr Cys Gly Ser Leu Arg Cys Leu Asn 1345 1350 1355 1360
- Gly Gly Thr Cys Ile Ser Gly Pro Arg Ser Pro Thr Cys Leu Cys Leu 1365 1370 1375
- Gly Pro Phe Thr Gly Pro Glu Cys Gln Phe Pro Ala Ser Ser Pro Cys 1380 1385 1390
- Leu Gly Gly Asn Pro Cys Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser 1395 1400 1405
- Glu Ser Pro Phe Tyr Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu 1410 1420
- Leu Cys His Ile Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp 1425 1430 1435 1440
- Ile Pro Pro Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln 1445 1450 1455
- Glu Asp Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala 1460 1465 1470
- Cys Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp 1475 1480 1485

- Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp Gly 1490 1495 1500
- His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp Gly Phe 1505 1510 1515 1520
- Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr Asp Gln Tyr 1525 1530 1535
- Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln Gly Cys Asn Ser
- Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala Glu His Val Pro Glu 1555 1560 1565
- Arg Leu Ala Ala Gly Thr Leu Val Val Val Leu Met Pro Pro Glu 1570 1580
- Gln Leu Arg Asn Ser Ser Phe His Phe Leu Arg Glu Leu Ser Arg Val 1585 1590 1595 1600
- Leu His Thr Asn Val Val Phe Lys Arg Asp Ala His Gly Gln Gln Met
 1605 1610 1615
- Ile Phe Pro Tyr Tyr Gly Arg Glu Glu Leu Arg Lys His Pro Ile 1620 1625 1630
- Lys Arg Ala Ala Glu Gly Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln
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- Val Lys Ala Ser Leu Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg 1650 1660
- Arg Glu Leu Asp Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu 1665 1670 1675 1680
- Ile Asp Asn Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser 1685 1690 1695
- Ala Thr Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser 1700 1705 1710
- Leu Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu 1715 1720 1725
- Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala 1730 1735 1740
- Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys 1745 1750 1760
- Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val 1765 1770 1775
- Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser 1780 1785 1790

- Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp 1795 1800 1805
- Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe 1810 - 1815 1820
- Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp Asp Gln Thr Asp 1825 1830 1835 1840
- His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met 1845 1850 1855
- Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys 1860 1865 1870
- Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile 1875 1880 1885
- Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu 1890 1895 1900
- Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser 1905 1910 1915 1920
- Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala 1925 1930 1935
- Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser 1940 1945 1950
- Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala 1955 1960 1965
- Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn 1970 1975 1980
- Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu 1985 1990 1995 2000
- Ile Leu Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile 2005 2010 2015
- Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala 2020 2025 2030
- Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Leu 2035 2040 2045
- Leu Lys Asn Gly Ala Asn Lys Asp Met Gln Asn Asn Arg Glu Glu Thr 2050 2055 2060
- Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala Lys Val 2065 2070 2075 2080
- Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg 2085 2090 2095

- Leu Pro Arg Asp Ile Ala Gln Glu Arg Met His His Asp Ile Val Arg 2100 2105 2110
- Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala 2115 2120 2125
- Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn 2130 2135 2140
- Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg 2145 2150 2155 2160
- Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp 2165 2170 2175
- Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu 2180 2185 2190
- Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His 2195 2200 2205
- Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro Phe 2210 2215 2220
- Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met Pro Asp 2225 2230 2235 2240
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- Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr Val Gly Gly Ser Thr Ser 2290 2295 2300
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- Ser Thr Gln Ala Pro Ser Leu Gln His Gly Met Val Gly Pro Leu His 2340 2345 2350
- Ser Ser Leu Ala Ala Ser Ala Leu Ser Gln Met Met Ser Tyr Gln Gly 2355 2360 2365
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- Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro 2385 2390 2395 2400

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- Gln Pro His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg 2420 2425 2430
- Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val Gln Pro Leu Gly 2435 2440 2445
- Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln Glu Ser Pro Ala 2450 2455 2460
- Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro Val Thr Ala Ala 2465 2470 2475 2480
- Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser Pro Val Asp 2485 2490 2495
- Asn Thr Pro Ser His Gln Leu Gln Val Pro Glu His Pro Phe Leu Thr 2500 2505 2510
- Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro His Ser 2515 2520 2525
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- Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His 50 55 60
- Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val 65 70 75 80
- Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe 85 90 95
- Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser 100 105 110

Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr 155 150 Thr Val Ala Asn Gln Phe Ser Cys Lys Cys Leu Thr Gly Phe Thr Gly Gln Lys Cys Glu Thr Asp Val Asn Glu Cys Asp Ile Pro Gly His Cys Gln His Gly Gly Thr Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln 200 Cys Pro Gln Gly Phe Thr Gly Gln Tyr Cys Asp Ser Leu Tyr Val Pro Cys Ala Pro Ser Pro Cys Val Asn Gly Gly Thr Cys Arg Gln Thr Gly Asp Phe Thr Phe Glu Cys Asn Cys Leu Pro Gly Phe Glu Gly Ser Thr 250 Cys Glu Arg Asn Ile Asp Asp Cys Pro Asn His Arg Cys Gln Asn Gly 260 Gly Val Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro 280 Gln Trp Thr Gly Gln Phe Cys Thr Glu Asp Val Asp Glu Cys Leu Leu Gln Pro Asn Ala Cys Gln Asn Gly Gly Thr Cys Ala Asn Arg Asn Gly 315 310 Gly Tyr Gly Cys Val Cys Val Asn Gly Trp Ser Gly Asp Asp Cys Ser Glu Asn Ile Asp Asp Cys Ala Phe Ala Ser Cys Thr Pro Gly Ser Thr Cys Ile Asp Arg Val Ala Ser Phe Ser Cys Met Cys Pro Glu Gly Lys 360 Ala Gly Leu Leu Cys His Leu Asp Asp Ala Cys Ile Ser Asn Pro Cys His Lys Gly Ala Leu Cys Asp Thr Asn Pro Leu Asn Gly Gln Tyr Ile 390 395 Cys Thr Cys Pro Gln Gly Tyr Lys Gly Ala Asp Cys Thr Glu Asp Val

- Asp Glu Cys Ala Met Ala Asn Ser Asn Pro Cys Glu His Ala Gly Lys 420 425 430
- Cys Val Asn Thr Asp Gly Ala Phe His Cys Glu Cys Leu Lys Gly Tyr 435 440 445
- Ala Gly Pro Arg Cys Glu Met Asp Ile Asn Glu Cys His Ser Asp Pro 450 460
- Cys Gln Asn Asp Ala Thr Cys Leu Asp Lys Ile Gly Gly Phe Thr Cys 465 470 475 480
- Leu Cys Met Pro Gly Phe Lys Gly Val His Cys Glu Leu Glu Ile Asn 485 490 495
- Glu Cys Gln Ser Asn Pro Cys Val Asn Asn Gly Gln Cys Val Asp Lys
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- Val Asn Arg Phe Gln Cys Leu Cys Pro Pro Gly Phe Thr Gly Pro Val 515 520 525
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- Gly Phe Thr Gly Val Leu Cys Glu Glu Asn Ile Asp Asn Cys Asp Pro 565 570 575
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- Cys Ile Cys Asn Pro Gly Tyr Met Gly Ala Ile Cys Ser Asp Gln Ile 595 600 605
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- Leu Val Asn Gly Tyr Gln Cys Asn Cys Gln Pro Gly Thr Ser Gly Val 625 630 635 640
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- Arg Cys Ile Cys Pro Glu Gly Pro His His Pro Ser Cys Tyr Ser Gln 705 710 715 720

- Val Asn Glu Cys Leu Ser Asn Pro Cys Ile His Gly Asn Cys Thr Gly 725 730 735
- Gly Leu Ser Gly Tyr Lys Cys Leu Cys Asp Ala Gly Trp Val Gly Ile 740 . 745 750
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- Tyr Thr Cys His Cys Val Leu Pro Tyr Thr Gly Lys Asn Cys Gln Thr 820 825 830
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- Lys Glu Ser Pro Asn Phe Glu Ser Tyr Thr Cys Leu Cys Ala Pro Gly 850 860
- Trp Gln Gly Gln Arg Cys Thr Ile Asp Ile Asp Glu Cys Ile Ser Lys 865 870 875 880
- Pro Cys Met Asn His Gly Leu Cys His Asn Thr Gln Gly Ser Tyr Met 885 890 895
- Cys Glu Cys Pro Pro Gly Phe Ser Gly Met Asp Cys Glu Glu Asp Ile 900 905 910
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- Gly Val Asn Thr Phe Ser Cys Leu Cys Leu Pro Gly Phe Thr Gly Asp 930 935 940
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 965 970 975
- Ala Gly Phe Asp Gly Val His Cys Glu Asn Asn Ile Asn Glu Cys Thr 980 985 990
- Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser 995 1000 1005
- Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys Leu His 1010 1015 1020

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- Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly Tyr Thr 1045 1050 1055
- Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser Pro Cys 1060 1065 1070
- Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln Cys Leu 1075 1080 1085
- Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn Val Ser 1090 1095 1100
- Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His Leu Cys 1105 1110 1115 1120
- Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr Cys Gln 1125 1130 1135
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- Glu Tyr Glu Val Asp Glu Cys Gln Asn Gln Pro Cys Gln Asn Gly Gly 1185 1190 1195 1200
- Thr Cys Ile Asp Leu Val Asn His Phe Lys Cys Ser Cys Pro Pro Gly 1205 1210 1215
- Thr Arg Gly Leu Leu Cys Glu Glu Asn Ile Asp Asp Cys Ala Arg Gly 1220 1225 1230
- Pro His Cys Leu Asn Gly Gly Gln Cys Met Asp Arg Ile Gly Gly Tyr 1235 1240 1245
- Ser Cys Arg Cys Leu Pro Gly Phe Ala Gly Glu Arg Cys Glu Gly Asp 1250 1255 1260
- Ile Asn Glu Cys Leu Ser Asn Pro Cys Ser Ser Glu Gly Ser Leu Asp 1265 1270 1275 1280
- Cys Ile Gln Leu Thr Asn Asp Tyr Leu Cys Val Cys Arg Ser Ala Phe 1285 1290 1295
- Thr Gly Arg His Cys Glu Thr Phe Val Asp Val Cys Pro Gln Met Pro 1300 1305 1310
- Cys Leu Asn Gly Gly Thr Cys Ala Val Ala Ser Asn Met Pro Asp Gly 1315 1320 1325

- Phe Ile Cys Arg Cys Pro Pro Gly Phe Ser Gly Ala Arg Cys Gln Ser 1330 1335 1340
- Ser Cys Gly Gln Val Lys Cys Arg Lys Gly Glu Gln Cys Val His Thr 1345 1350 1355 1360
- Ala Ser Gly Pro Arg Cys Phe Cys Pro Ser Pro Arg Asp Cys Glu Ser 1365 1370 1375
- Gly Cys Ala Ser Ser Pro Cys Gln His Gly Gly Ser Cys His Pro Gln 1380 1385 1390
- Arg Gln Pro Pro Tyr Tyr Ser Cys Gln Cys Ala Pro Pro Phe Ser Gly 1395 . 1400 1405
- Ser Arg Cys Glu Leu Tyr Thr Ala Pro Pro Ser Thr Pro Pro Ala Thr 1410 1415 1420
- Cys Leu Ser Gln Tyr Cys Ala Asp Lys Ala Arg Asp Gly Val Cys Asp 1425 1430 1435 1440
- Glu Ala Cys As
n Ser His Ala Cys Gl
n Trp Asp Gly Gly Asp Cys Ser 1445 1450 1455
- Leu Thr Met Glu Asn Pro Trp Ala Asn Cys Ser Ser Pro Leu Pro Cys 1460 1465 1470
- Trp Asp Tyr Ile Asn Asn Gln Cys Asp Glu Leu Cys Asn Thr Val Glu 1475 1480 1485
- Cys Leu Phe Asp Asn Phe Glu Cys Gln Gly Asn Ser Lys Thr Cys Lys 1490 1495 1500
- Tyr Asp Lys Tyr Cys Ala Asp His Phe Lys Asp Asn His Cys Asn Gln 1505 1510 1515 1520
- Gly Cys Asn Ser Glu Glu Cys Gly Trp Asp Gly Leu Asp Cys Ala Ala 1525 1530 1535
- Asp Gln Pro Glu Asn Leu Ala Glu Gly Thr Leu Val Ile Val Val Leu 1540 1545 1550
- Met Pro Pro Glu Gln Leu Gln Asp Ala Arg Ser Phe Leu Arg Ala 1555 1560 1565
- Leu Gly Thr Leu Leu His Thr Asn Leu Arg Ile Lys Arg Asp Ser Gln 1570 1580
- Gly Glu Leu Met Val Tyr Pro Tyr Tyr Gly Glu Lys Ser Ala Ala Met 1585 1590 1595 1600
- Lys Lys Gln Arg Met Thr Arg Arg Ser Leu Pro Gly Glu Gln Glu Gln 1605 1615
- Glu Val Ala Gly Ser Lys Val Phe Leu Glu Ile Asp Asn Arg Gln Cys 1620 1625 1630

- Val Gln Asp Ser Asp His Cys Phe Lys Asn Thr Asp Ala Ala Ala 1635 $1640 \hspace{1.5cm} 1645$
- Leu Leu Ala Ser His Ala Ile Gln Gly Thr Leu Ser Tyr Pro Leu Val 1650 1660
- Ser Val Val Ser Glu Ser Leu Thr Pro Glu Arg Thr Gln Leu Leu Tyr 1665 1670 1680
- Leu Leu Ala Val Ala Val Val Ile Ile Leu Phe Ile Ile Leu Leu Gly
 1685 1690 1695
- Val Ile Met Ala Lys Arg Lys Arg Lys His Gly Ser Leu Trp Leu Pro 1700 1705 1710
- Glu Gly Phe Thr Leu Arg Arg Asp Ala Ser Asn His Lys Arg Arg Glu 1715 1720 1725
- Pro Val Gly Gln Asp Ala Val Gly Leu Lys Asn Leu Ser Val Gln Val 1730 1735 1740
- Ser Glu Ala Asn Leu Ile Gly Thr Gly Thr Ser Glu His Trp Val Asp 1745 1750 1755 1760
- Asp Glu Gly Pro Gln Pro Lys Lys Val Lys Ala Glu Asp Glu Ala Leu 1765 1770 1775
- Leu Ser Glu Glu Asp Asp Pro Ile Asp Arg Pro Trp Thr Gln Gln 1780 1785 1790
- His Leu Glu Ala Ala Asp Ile Arg Arg Thr Pro Ser Leu Ala Leu Thr 1795 1800 1805
- Pro Pro Gln Ala Glu Gln Glu Val Asp Val Leu Asp Val Asn Val Arg 1810 1815 1820
- Gly Pro Asp Gly Cys Thr Pro Leu Met Leu Ala Ser Leu Arg Gly Gly 1825 1830 1835 1840
- Ser Ser Asp Leu Ser Asp Glu Asp Glu Asp Ala Glu Asp Ser Ser Ala 1845 1850 1855
- Asn Ile Ile Thr Asp Leu Val Tyr Gln Gly Ala Ser Leu Gln Ala Gln 1860 1865 1870
- Thr Asp Arg Thr Gly Glu Met Ala Leu His Leu Ala Ala Arg Tyr Ser 1875 1880 1885
- Arg Ala Asp Ala Ala Lys Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn 1890 1895 1900
- Ala Gln Asp Asn Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala 1905 1910 1915 1920
- Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Val Thr Asp 1925 1930 . 1935

- Leu Asp Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala 1940 1945 1950
- Arg Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala 1955 1960 1965
- Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp Ala 1970 1975 1980
- Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Leu Lys Asn Gly 1985 1990 1995 2000
- Ala Asn Arg Asp Met Gln Asp Asn Lys Glu Glu Thr Pro Leu Phe Leu 2005 2010 2015
- Ala Ala Arg Glu Gly Ser Tyr Glu Ala Ala Lys Ile Leu Leu Asp His 2020 2025 2030
- Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp 2035 2040 2045
- Val Ala Arg Asp Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu 2050 2055 2060
- Tyr Asn Val Thr Pro Ser Pro Pro Gly Thr Val Leu Thr Ser Ala Leu 2065 2070 2075 2080
- Ser Pro Val Ile Cys Gly Pro Asn Arg Ser Phe Leu Ser Leu Lys His 2085 2090 2095
- Thr Pro Met Gly Lys Lys Ser Arg Arg Pro Ser Ala Lys Ser Thr Met 2100 2105 2110
- Pro Thr Ser Leu Pro Asn Leu Ala Lys Glu Ala Lys Asp Ala Lys Gly 2115 2120 2125
- Ser Arg Arg Lys Lys Ser Leu Ser Glu Lys Val Gln Leu Ser Glu Ser 2130 2135 2140
- Ser Val Thr Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Thr Tyr 2145 2150 2155 2160
- Val Ser Asp Thr Thr Ser Ser Pro Met Ile Thr Ser Pro Gly Ile Leu 2165 2170 2175
- Gln Ala Ser Pro Asn Pro Met Leu Ala Thr Ala Ala Pro Pro Ala Pro 2180 2185 2190
- Val His Ala Gln His Ala Leu Ser Phe Ser Asn Leu His Glu Met Gln 2195 2200 2205
- Pro Leu Ala His Gly Ala Ser Thr Val Leu Pro Ser Val Ser Gln Leu 2210 2215 2220
- Leu Ser His His His Ile Val Ser Pro Gly Ser Gly Ser Ala Gly Ser 2225 2230 2235 2240

Leu Ser Arg Leu His Pro Val Pro Val Pro Ala Asp Trp Met Asn Arg 2245 2250 2255

Met Glu Val Asn Glu Thr Gln Tyr Asn Glu Met Phe Gly Met Val Leu 2260 2265 2270

Ala Pro Ala Glu Gly Thr His Pro Gly Ile Ala Pro Gln Ser Arg Pro 2275 2280 2285

Pro Glu Gly Lys His Ile Thr Thr Pro Arg Glu Pro Leu Pro Pro Ile 2290 2295 2300

Val Thr Phe Gln Leu Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly 2305 2310 2315 2320

Ala Pro Gln Pro Gln Ser Thr Cys Pro Pro Ala Val Ala Gly Pro Leu 2325 2330 2335

Pro Thr Met Tyr Gln Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala $2340 \\ 2345 \\ 2350$

Phe Pro Thr Ala Met Met Pro Gln Gln Asp Gly Gln Val Ala Gln Thr 2355 2360 2365

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Ala Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala 2435 2440 2445

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Ser Arg Gln Arg Gly Glu Val Arg Phe Val Gln Tyr Asp Glu Ser Asp

Ala Pro Thr Arg Ser Lys Thr Pro Ala Gln Gly Leu Ala Arg Lys Leu 165 170 175

His Phe Ser Thr Ala Pro Pro Asn Pro Asp Ala Pro Trp Thr Pro Arg 180 185 190

Val Ala Gly Phe Asn Lys Arg Val Phe Cys Ala Ala Val Gly Arg Leu 195 200 205

Ala Ala Met His Ala Arg Met Ala Ala Val Gln Leu Trp Asp Met Ser 210 215 220

Arg Pro Arg Thr Asp Glu Asp Leu Asn Glu Leu Leu Gly Ile Thr Thr 225 230 235 240

Ile Arg Val Thr Val Cys Glu Gly Lys Asn Leu Leu Gln Arg Ala Asn 245 250 255

Glu Leu Val Asn Pro Asp Val Val Gln Asp Val Asp Ala Ala Thr Ala 260 265 270

Thr Arg Gly Arg Ser Ala Ala Ser Arg Pro Thr Glu Arg Pro Arg Ala 275 280 285

Pro Ala Arg Ser Ala Ser Arg Pro Arg Arg Pro Val Glu 290 295 300